

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH**

**215th Meeting of the
NATIONAL DIABETES AND DIGESTIVE AND KIDNEY DISEASES ADVISORY COUNCIL
DIVISION OF DIGESTIVE DISEASES AND NUTRITION SUBCOMMITTEE
Meeting Summary**

**Thursday, January 28, 2021
Zoom Video Conference**

Open Session

- 1) Dr. Stephen James opened the meeting by welcoming everyone, introducing new DDDN Program Director, Dr. Katrina Loh and announcing the retirement of DDDN Program Director, Dr. Robert Karp.
- 2) The minutes of the September 9, 2020 subcommittee meeting were approved.
- 3) Dr. James provided a summary of the DDDN FY2020 portfolio.

Note: During the Open Session of Full Council, Dr. Griffin Rodgers announced that the Office of Nutrition Research (ONR) will be moving from DDDN to the Office of the Director (OD).

In response to how DDDNs nutrition grants will be affected once ONR moves from DDDN to OD, it was explained that ONR did not formally award grants, therefore, all nutrition related grant awards will remain with DDDN and all divisions within NIDDK will continue to support nutrition.

- 4) Dr. David Saslowsky reviewed three DDDN Funding Opportunity Announcements.
Question: Where did the concept to not allow preliminary data on Stephen I. Katz R01 (Early Stage Investigators) applications come from?
Answer: Eliminating preliminary data in these R01 applications gives ESI who may not have as much experience a better chance of being awarded.
Question: Can a K-awardee apply for the Stephen I. Katz R01 (Early Stage Investigators) mechanism?
Answer: If the R01 application is a pivot (still being defined) away from the research being done through the K-award.
Question: Regarding health equity, is this something that can be woven into the Steven I. Katz R01 (Early Stage Investigators) mechanism?
Answer: Yes
- 5) Dr. Aynur Unalp-Arida presented changes and updates to NIDDK support of Clinical Studies.
- 6) Dr. Saslowsky introduced the purpose and focus of the Digestive Diseases Interagency Coordinating Committee (DDICC). The DDICC facilitates cooperation, information exchange, and collaboration across interested NIH Institutes and partnering Federal agencies to provide a structure for coordinated efforts to combat digestive diseases.

Question: How can one access one of the upcoming DDICC meetings?

Answer: The current plan is to send targeted invitations; council members will be included.

Question: Will other ICs be invited to the DDICC meetings?

Answer: Absolutely.

Question: How many DDICC meetings are being planned per year?

Answer: The frequency of meetings has not been determined yet; it is possible to have a few a year and can be based on how many ideas are brought to the table.

7) Dr. Jay Hoofnagle presented an overview on the LiverTox database.

Question: Can the LiverTox website track how many times it is accessed by people outside of the United States?

Answer: We recently made this request to the website administrators as questions come in from around the world.

Question: Does LiverTox track visits to the site by medical professionals versus the general population?

Answer: Currently the site does not track this, but a survey is being generated to obtain this information.

Question: How are the herbals and supplements chosen to be included on LiverTox?

Answer: Herbals and supplements known to cause liver injury are selected first, followed by those most commonly used.

8) Dr. Saslowsky presented an overview of the F/K and Loan Repayment Program funding dynamics.

Question: The F31s have a diversity component while the F30s and F32s do not. Why is this?

Answer: This is a good question that we will have to investigate. A response will be provided when available.

9) Dr. Terez Shea-Donohue presented the Celiac Disease Portfolio Analysis.

10) Three DDDN Initiative Concept Clearances were presented during the Open Session of the Full Council (more details on the clearances can be found in the appendix):

- a) Advancing Early Stage Investigator-Led Mechanistic Research on HIV Comorbidities, Coinfections, and Complications (New)
- b) Silvio O. Conte Digestive Diseases Research Core Centers (Renewal)
- c) Nutrition Obesity Research Center (NORC) Program (Renewal)

11) Planned Workshops (more details can be found in the appendix):

a) **Accelerating Progress in Celiac Disease (CD)** will be held virtually March 18-19, 2021. The objectives of the workshop are to:

- Bring together investigators interested in understanding CD pathophysiology and treatment options.
- Evaluate current understanding of CD pathogenesis, with special consideration of mechanisms.
- Identify barriers hindering progress, emerging areas and gaps in knowledge, and novel diagnostics and therapeutics for patients with CD.
- Facilitate crosstalk among NIDDK and NIAID program staff to enhance partnerships opportunities for supporting CD research.

b) **Understanding of Risk and Causal Mechanisms for Developing Obesity in Infants and Young Children** will be held virtually on April 29, 2021. The objectives of the workshop are to learn:

- What is known regarding the epidemiology/risk factors and underlying biological and behavioral mechanisms for rapid weight gain and development of obesity in early life.
- What new approaches, such as the use of integrated omics can be used to improve risk prediction and gain novel insights into the causes of obesity in early life.

Closed Session

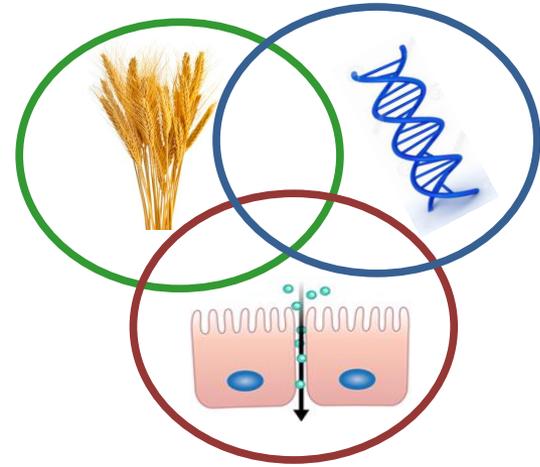
Council members reviewed competing applications; three applicants with >\$1M in NIH funding (direct costs) and three budget restorations. There were no appeals, foreign applications or skipped applications to review. In all discussions, Council members concurred with NIDDK/DDDN.

Comments and critiques regarding discussion topics and initiatives from council members are welcome and should be emailed to Drs. James and Saslowsky in advance of the meeting.

-Appendix-

Planned Workshops

Joint NIDDK-NIAID Workshop



Accelerating Progress in Celiac Disease

Virtual Meeting
March 18-19, 2021

Patricia Greenwel (NIDDK)
Annette Rothermel (NIAID)
Terez-Shea Donohue (NIDDK)



Accelerating Progress in Celiac Disease

Meeting Co-Chairs:

- Alessio Fasano (Massachusetts General Hospital)
- Andrei Ivanov (Cleveland Clinic)
- Joseph Murray (Mayo Clinic, Rochester)

NIH Organizing Committee:

- Patricia Greenwel (NIDDK)
- Annette Rothermel (NIAID)
- Terez Shea-Donohue (NIDDK)



Introduction

Background: Celiac disease (CD) is one of the most common autoimmune diseases, with a prevalence of approximately 1% in the Western population, that requires dietary exposure to gluten in genetically predisposed individuals. Exposure to gluten leads to the activation of both the innate and adaptive immune responses and subsequent chronic inflammation.

Rationale: CD prevalence is increasing worldwide, for reasons that are currently unknown. However, progress in understanding CD pathophysiology has been hampered due to misconceptions regarding effectiveness of gluten-free diets, limited studies in populations outside USA and Europe, and lack of reliable and reproducible animal models.

Objectives

- To bring together investigators interested in understanding CD pathophysiology and treatment options
- To evaluate current understanding of CD pathogenesis, with special consideration of mechanisms
- To identify barriers hindering progress, emerging areas and gaps in knowledge, and novel diagnostics and therapeutics for patients with CD
- To facilitate cross-talk among NIDDK and NIAID program staff to enhance partnerships opportunities for supporting CD research

Agenda

- **Keynote Topics:**

- **Celiac Disease Overview**

- Celiac disease: The spectrum of disease and its outcomes
 - Patient viewpoint
 - How does celiac disease fit into the spectrum of autoimmune diseases
 - Genetics of celiac disease: from GWAS to single cell RNAseq

- **Modeling Celiac Disease**

- 4 Talks and Q&A Panel discussion

- **Immunology of Celiac Disease**

- 4 Talks and Q&A Panel discussion

- **Emerging Areas in Celiac Disease**

- 4 Talks and Q&A Panel discussion

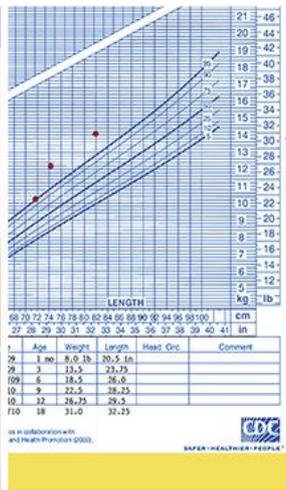
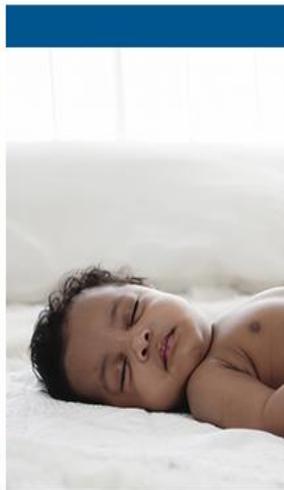
- **Diagnostics and Therapeutics for Celiac Disease**

- 5 Talks and Q&A Panel discussion

4 Breakout sessions – Session leaders to discuss and report on summary of research gaps and opportunities in this area. Invited participants include senior leaders in the field as well as junior and early-stage investigators who are working in areas related to this workshop.

Understanding of Risk and Causal Mechanisms for Developing Obesity in Infants and Young Children

A Virtual Workshop



April 29, 2021 10:00–3:00 p.m. ■ April 30, 2021 10:00–2:30 p.m.

Voula Osganian, M.D., Sc.D.



Leadership

Meeting Co-Chairs

- Shari L. Barkin, M.D., M.S.H.S., *Vanderbilt University School of Medicine*
- Charles F. Burant, M.D., Ph.D., *University of Michigan School of Medicine*
- Susan Carnell, Ph.D., *Johns Hopkins University School of Medicine*

NIH Organizing Committee

- Voula Osganian, M.D., Sc.D., M.P.H. and Susan Yanovski, M.D., *National Institutes of Diabetes and Digestive and Kidney Diseases*
- Andrew Bremer, M.D., Ph.D., M.A.S. and Ashley Vargas, Ph.D., M.P.H., R.D.N, *Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health*
- Charlotte Pratt, Ph.D., R.D., *National Heart, Lung, and Blood Institute*
- Christine Hunter, Ph.D., ABPP Deborah Young-Hyman, Ph.D., *Office of Behavioral and Social Sciences Research*
- Jacqueline Lloyd, Ph.D., M.S.W., *Office of Disease Prevention*

Background & Objectives

Background/Rationale

The prevalence of obesity in children remains high and is increasing. Accelerated growth patterns during infancy and early childhood are associated with a higher risk of overweight or obesity in later life. These early high-risk growth trajectories tend to persist, suggesting this is a critical period for intervention. Yet, most interventions show only modest favorable changes in body mass index (BMI) that are not sustained, and current risk prediction models that incorporate known gene variants, maternal risk factors, and other early life risk factors are not accurate enough to distinguish who will/will not develop obesity. The complex mechanisms that underlie how these various risk factors contribute to adiposity are not well understood and need investigation.

Objectives

- What is known regarding the epidemiology/risk factors and underlying biological and behavioral mechanisms for rapid weight gain and development of obesity in early life.
- What new approaches, such as the use of integrated omics can be used to improve risk prediction and gain novel insights into the causes of obesity in early life.

Agenda - Day 1

Session 1: State of Childhood Obesity Prevention

Risk and Causal Factors for Accelerated Growth Trajectories and Development of Obesity

Lori A Francis, Ph.D., The Pennsylvania State University

Overview of Obesity Prevention Trials for Infants and Young Children- Lessons Learned

Ihuoma Eneli, M.D., M.S., F.A.A.P., The Ohio State University College of Medicine

Moderated Discussion

Amelie G. Ramirez, Dr.P.H., M.P.H., UT Health, Lozano Long School of Medicine, San Antonio, Texas

Session 2: Biological and Behavioral Mechanisms: Pregnancy and the In-Utero Environment

Maternal & Paternal Risk Factors/Fetal Programming and Epigenetic Mechanisms

Kjersti Marie Aagaard, M.D., Ph.D., F.A.C.O.G., Baylor College of Medicine

Nutrition during Pregnancy

Linda Van Horn, Ph.D., R.D., Northwestern University Feinberg School of Medicine

Environmental Exposures During Pregnancy

Leonardo Trasande, M.D., M.P.P., New York University Grossman School of Medicine

Moderated Discussion

Marie-France-Hivert, M.D., M.M.Sc., Harvard Medical School

Agenda - Day 2

Sessions 3 and 4 : Biological and Behavioral Mechanisms- Infancy through Early Childhood

The Exposome and Obesity <i>Rosalind Wright, M.D., M.P.H., Icahn School of Medicine at Mount Sinai, New York</i>
Genetic Predisposition and Polygenic Risk <i>Ruth Loos, Ph.D., Icahn School of Medicine at Mount Sinai, New York</i>
Nutrition, the Gut Microbiome, and Growth: Associations vs. Causality <i>Sharon Donovan, Ph.D., R.D., University of Illinois, Urbana-Champaign</i>
Human Milk Composition, Complementary Foods and Growth and Body Composition <i>Ellen Demerath, Ph.D., University of Minnesota</i>
Moderated Discussion <i>Melissa Wake, MB.ChB., M.D. F.A.H.M.S., University of Melbourne, Australia</i>
Appetite and Eating Behaviors <i>Diane Gilbert-Diamond, Sc.D., Dartmouth Geisel School of Medicine</i>
Temperament, Self -Regulation, and Executive Function <i>Alison Miller, Ph.D., University of Michigan</i>
Sleep and Circadian Rhythm <i>Monique K. LeBourgeois, Ph.D., M.A., M.S., University of Colorado at Boulder</i>
24-hr movement behaviours (physical activity, sedentary behavior, and sleep) <i>Anthony Okely, Ed.D., University of Wollongong, Australia</i>
Moderated Discussion <i>Julie Lumeng, M.D., University of Michigan</i>

Agenda

- Early Investigator Lightning Talks and Virtual Poster Session
- Panel Discussion with key questions to be addressed
 - What are the **research gaps** that need to be addressed to improve our understanding of the causal mechanisms by which individual children are at higher or lower risk for accelerated growth trajectories and the development of obesity in the early years?
 - For which **specific populations** should research on risk and causal mechanisms be prioritized? This could include but is not limited to developmental stage/critical period of risk; families with a strong family history of obesity; children with severe obesity; at-risk populations, such as racial and ethnic minority populations or children/families of low SES.
 - What **research approaches** will improve our understanding of the causal mechanisms by which individual children are at higher or lower risk for accelerated growth trajectories and the development of obesity in the early years, consider new paradigms, study designs, study sample characteristics, definition and measurement of outcomes, and use of assessment methodologies or technologies.
 - What are the **challenges, acceptability and feasibility** of obtaining biospecimens/tissue samples, imaging, and other relevant metabolic, biobehavioral, and environmental measures in real-time and at sensitive time periods from mothers, infants, young children, and families? What are strategies to overcome them?
- Register at <https://www.niddk.nih.gov/news/meetings-workshops/2021/think-tank-meeting>

January 2021 Advisory Council

DDN Concept Clearances

January 2021 DDN Concept Clearances

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Advancing Early Stage Investigator-Led Mechanistic Research on HIV Comorbidities, Coinfections, and Complications

Lead Division / Office: DDN, DEM, KUH

Point(s) of Contact: Peter Perrin, DDN

Executive Summary:

Progress toward preventing or treating HIV comorbidities, coinfections, and complications requires a thriving community of researchers with expertise at the intersection of HIV science with the biology of organs, tissues, and processes. Fostering Early Stage Investigators (ESIs) is critical for that community's long-term stability. This initiative therefore seeks to encourage and support talented ESIs pursuing mechanistic biological research on HIV CCCs within the mission of the NIDDK.

The Need / Background:

Although there has been significant progress in effective viral suppression with antiretroviral therapies, HIV comorbidities, coinfections, and complications (CCCs) remain an important public health problem. Important HIV CCCs within the NIDDK's mission include enteropathy and loss of gastrointestinal homeostasis; noncommunicable liver diseases and viral hepatitis coinfections; kidney, urologic, and hematologic diseases; and obesity, diabetes, and associated complications. Moreover, NIDDK-relevant pathogenic processes, such as enteropathy, may contribute to HIV pathogenesis in other tissues and organ systems. Obesity can have multiple pathophysiological and metabolic consequences throughout the body. Development of preventive and therapeutic modalities requires in-depth mechanistic interrogation of the biological basis of HIV CCCs.

The Opportunity:

Research designed to decrease and/or manage HIV CCCs is one of the research priorities enumerated in the "NIH Strategic Plan for HIV and HIV-Related Research" for FY2021-2025. CCCs will continue to impact the health and well-being of people with HIV (PWH) throughout the lifespan for the foreseeable future. Even after the development of an effective sterile cure, pathology will persist in people who have developed CCCs. Indeed, their CCCs may continue to worsen. While many of the HIV CCCs also occur in people without HIV, there are important and unique biological mechanisms underlying their development in the context of HIV. Chronic infection, long-term antiretroviral therapy use, and aging all contribute to the development of CCCs in PWH. Moreover, as the HIV pandemic progresses, new CCCs may emerge. Therefore, it is imperative to foster the long-term growth and stability of a community of talented investigators at the intersection of HIV science with physiology, metabolism, and pathobiology within the mission of the NIDDK.

The Proposed Approach:

HIV CCCs will continue to present a public health problem that impacts the well-being of PWH in

the long term. This initiative is an important element of a larger effort to maintain a rigorous community of investigators dedicated to interrogating the biological basis of CCCs. Encouraging and supporting ESIs who bring talent and creativity to the NIDDK's portfolio in this area is critical for future progress toward preventing or alleviating them as well as for confronting emerging challenges. This initiative will provide an opportunity for talented and creative ESIs to obtain independent funding at this vulnerable stage of their careers.

Expected Annual Expenditures: >\$1M to <\$5M

Silvio O. Conte Digestive Diseases Research Core Centers

Lead Division / Office: DDN

Point(s) of Contact: Peter Perrin, DDN

Executive Summary:

The Silvio O. Conte Digestive Diseases Research Core Centers (DDRCC) program seeks to promote synergy between established investigators engaged in digestive and/or liver diseases research at domestic research institutions. Each DDRCC supports a cohesive research base consisting of basic and clinical investigators actively conducting research related to an organizing theme. Both the theme and the structure should promote impactful multidisciplinary collaboration. This is accomplished through biomedical research cores, a pilot and feasibility program, and an enrichment program.

The Need / Background:

Collaborative multidisciplinary interactions greatly benefit progress toward understanding mechanisms underlying digestive and liver diseases and their translation into clinical practice. Center core grant programs, such as the long-established Silvio O. Conte Digestive Diseases Research Core Centers (DDRCC), foster these interactions by providing resources to strengthen the quality and cost effectiveness of research carried out by communities of independently funded investigators at institutions or consortia of institutions. The DDRCC program provides access to specialized technical resources, services, and other expertise through biomedical research cores. Pilot and Feasibility Programs foster the development of new ideas, especially by junior investigators or established investigators who are new to digestive and liver diseases research. Enrichment Program activities utilize various approaches to assisting trainee and both junior and senior investigators accomplish the DDRCC's goal.

Outcomes of Prior Initiative Cycles:

Silvio O. Conte Digestive Diseases Research Core Centers (DDRCCs) awards have provided support across the United States to communities of researchers involved in diverse areas of research. For example, some have been devoted to liver research exclusively, some have topics related to the luminal gastrointestinal tract, some have pancreas research components, and some have themes related to processes that are cross-cutting. The applicant-initiated approach to the theme has therefore broadly benefited NIDDK's digestive and liver disease research portfolio.

The Opportunity:

The Silvio O. Conte Digestive Diseases Research Core Centers is a long-established program that facilitates digestive and liver diseases research across the United States. The DDRCCs promote new discoveries and enhance scientific progress through shared resources that provide specialized technical resources, services, and/or expertise; pilot and feasibility programs that support the development of new research projects; and enrichment programs that enhance the research environment.

Each DDRCC is organized around a common research theme so that the biomedical research

cores, the pilot and feasibility program, and the enrichment program can be structured to meet the needs of the digestive and liver disease researchers who constitute the membership and to foster multidisciplinary interactions and collaborations, including those between basic and clinical researchers. The DDRCC's theme must be in an area of digestive and/or liver diseases within the mission of the NIDDK, and it is determined by the applicant based on the need of the DDRCC's membership. Because of this, a broad range of digestive and liver diseases research has benefited from this program.

The Proposed Approach:

This initiative seeks to continue the Silvio O. Conte Digestive Diseases Research Core Centers as currently constructed with opportunities each Fiscal Year for the duration of this initiative that invites both new and competing renewal applications.

Expected Annual Expenditures: >\$5M

Nutrition Obesity Research Center (NORC) Program

Lead Division / Office: DDN

Point(s) of Contact: Mary Evans, DDN

Executive Summary:

The Nutrition Obesity Research Centers (NORC) program has been an ongoing program for almost 40 years with support for 12 NORCs across the US. The NORCs promote new discoveries and enhance scientific progress through support of cutting-edge basic, clinical, and translational research related to nutrition science and/or obesity. The goal of the NORCs is to serve as a key component of the overall NIH/NIDDK plan to advance the fields of nutrition science and obesity and improve health of Americans across the lifespan. NORCs are intended to improve the quality and multidisciplinary nature of research on nutrition and obesity by providing shared access to specialized and technical resources and expertise. NORCs facilitate progress in research with the goal of developing new methods to evaluate, prevent, and treat obesity and to support basic and clinical nutrition science and dietary interventions. The NORCs are part of an integrated program of nutrition and obesity research. NORCs support extramural research institutions that have established an existing base of high-quality, nutrition and obesity-related research. NORCs provide increased, cost effective collaboration among multidisciplinary groups of investigators at institutions with an established, comprehensive research base in nutrition and obesity.

The Need / Background:

The mission of the NORC program is to serve as a key component of the NIDDK-supported research effort to advance nutrition and obesity research. The NORCs promote new discoveries and enhance scientific progress through support of cutting-edge basic, clinical, and translational research in nutrition science and obesity with the ultimate goal of improving public health.

To accomplish this mission, the NORCs:

- Create an environment that supports important and innovative research;
- Attract and retain early stage investigators and investigators new to nutrition/obesity research;
- Provide core services that leverage funding and unique expertise;
- Foster interdisciplinary collaborations, especially in emerging areas of research, to catalyze new ideas and scientific approaches;
- Raise awareness and interest in fundamental and clinical nutrition and/or obesity research at their institutions, as well as locally, regionally, and nationally;
- Promote the translation of scientific discoveries from bench to bedside to community to improve public health; and
- Enhance nutrition and obesity research education and training opportunities.

Outcomes of Prior Initiative Cycles:

NIDDK has supported the NORC program for close to 40 years. NORCs submit new or competitive renewals every 5 years with the expectation that applicants will demonstrate the

strength of their research base, usage and evolution of core services, productivity of the NORC user base, and the accomplishments of their pilot and feasibility program recipients.

The Opportunity:

The NORC program is intended to bring together investigators from a variety of scientific disciplines in a manner that enhances and extends the effectiveness of their research. A NORC must be an identifiable unit within a single or a consortium of cooperating institutions, including affiliated universities, medical centers, and/or other research organizations; however, NORCs may also foster interactions and collaborations between investigators at multiple institutions to promote a multifaceted approach to a common goal. In either case, NORC applications must be associated with an existing program of excellence as evidenced by a consistent and outstanding record of productivity and peer-reviewed research funding in the areas of nutrition and/or obesity. NORC funding will provide support for core facilities (shared resources), pilot and feasibility studies, and program enrichment activities. Except for pilot and feasibility studies, NORC funds are not intended to fund or otherwise support individual biomedical or behavioral research projects other than through core usage.

The Proposed Approach:

A P30 RFA will be issued inviting applications from institutions/organizations that propose to establish Centers as an integrated and existing program of nutrition and/or obesity research. The Nutrition Obesity Research Centers (NORC) program is designed to support and enhance the national research effort in nutrition and obesity. NORCs support three primary research-related activities: Research Core services, a Pilot and Feasibility (P and F) program, and an Enrichment program. All activities pursued by Nutrition Obesity Research Centers are designed to enhance the efficiency, productivity, effectiveness and multidisciplinary nature of research in nutrition and obesity. The NIDDK Nutrition Obesity Research Centers program consists of up to 12 Centers, each located at outstanding research institutions with documented programs of excellence in nutrition and/or obesity research.

Expected Annual Expenditures: >\$1M to <\$5M